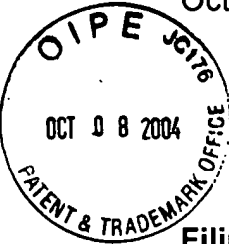


SPW

October 7, 2004

Micheline Gravelle B.Sc., M.Sc. (Immunology)  
416 957 1682 mgravelle@bereskinparr.com

Your Reference: 10/688,962  
Our Reference: 9579-80



**Filing of an Information Disclosure Statement**

Commissioner of Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450  
U.S.A

Dear Sirs:

**Re: United States Patent Application No. 10/688,962**  
**Filed: October 21, 2003**  
**Entitled: Modulators of fgl2 Prothrombinase**  
**Applicant: Trillium Therapeutics Inc.**  
**Examiner: Shanon A. Foley**  
**Art Unit: 1648**

---

In accordance with 37 CFR 1.97 and 1.98, and in recognition of the duty of disclosure set forth in 37 CFR 1.56, Applicant hereby submits an Information Disclosure Statement on Form PTO/SB/08a containing a listing of patents and other publications of which Applicant is aware. Applicant is also submitting the references listed on the Information Disclosure Statement.

All of the patents and publications submitted herewith are in the English language. Accordingly a concise explanation of the relevance of the documents is not required.

The Examiner is requested to indicate consideration of these documents by initialling the appropriate column.

Applicant reserves the right to contest the applicability of any of these documents as prior art against the subject application. If the Examiner has any questions concerning this Information Disclosure Statement, he/she is requested to contact the undersigned. Entry of the enclosed Information Disclosure Statement is believed to be in order and is respectfully requested.

*Please send all correspondence to the Toronto office:*

Scotia Plaza, 40 King St. West, 40th Floor,  
Toronto, Ontario, Canada M5H 3Y2  
Tel: 416.364.7311 Fax: 416.361.1398


2000 Argentia Rd., Plaza 4, Ste. 430,  
Mississauga, Ontario, Canada L5N 1W1  
Tel: 905.812.3600 Fax: 905.814.0031

Waterloo Technology Campus, 408 Albert St., Ste. 2,  
Waterloo, Ontario, Canada N2L 3V3  
Tel: 519.783.3210 Fax: 519.783.3211

This Information Disclosure Statement is being filed before the issuance of a first official action, and therefore no fees are required. However, please charge our deposit account No. 02-2095 if any fee is required.

Respectfully submitted,

**Trillium Therapeutics Inc.**

A handwritten signature in cursive script, appearing to read "M Gravelle", written over a horizontal line.

Micheline Gravelle

Registration No. 40,261

MG/aw

Encl.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/PTO

# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

**(Use as many sheets as necessary)**

Sheet 1 of 4

## U.S. PATENT DOCUMENTS

[illegible]

## FOREIGN PATENT DOCUMENTS

[illegible]

**Examiner  
Signature**

Date Considered

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. <sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> See Kinds Codes of USPTO Patent Documents at [www.uspto.gov](http://www.uspto.gov) or MPEP 901.04. <sup>3</sup> Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). <sup>4</sup> For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. <sup>5</sup> Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. <sup>6</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.97 and 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 2 hours to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

***If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.***

Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Sheet

2

of

4

**Complete if Known**

Application Number	10/688,962
Filing Date	October 21, 2003
First Named Inventor	Gary Levy
Art Unit	1648
Examiner Name	Shanon A. Foley
Attorney Docket Number	9579-80

**NON PATENT LITERATURE DOCUMENTS**

Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	1	Ning et al. "The Nucleocapsid Protein of Murine Hepatitis Virus Type 3 Induces Transcription of the Novel fgl2 Prothrombinase Gene", The Journal of Biological Chemistry, vol. 274, no. 15, 9 April 1999, pages 9930-9936, XP002144400, ISSN: 0021-9258	
	2	Stohlman SA, Bergmann C, Cua D, Wege H, van der Veen R. Location of antibody epitopes within the mouse hepatitis virus nucleocapsid protein. Virology. 1994 Jul; 202(1):146-53.	
	3	Mizutani T, Maeda A, Hayashi M, Isogai H, Namioka S. Both antisense and sense RNAs against the nucleocapsid protein gene inhibit the multiplication of mouse hepatitis virus. J Vet Med Sci. 1994 Apr;56(2):211-5.	
	4	Ding JW et al. Cloning and characterization of the human prothrombinase gene (H-fgl2) and its role in human hepatitis. Hepatology vol. 28, no. 4 Part 2, October 1998 (1998-10), page 254A	
	5	Levy Gary et al. "Study of Putative Cis-Elements in MFGL2 Promoter in Response to Nucleocapsid Protein of Murine Hepatitis Virus Type 3", Hepatology, vol. 30, no. 4 Part 2, October 1999, page 502A	
	6	Cattral MS, Levy GA. Artificial liver support--pipe dream or reality? N Engl J Med. 1994 Jul 28;331(4):268-9. No abstract available.	
	7	Chisari FV, Ferrari C. Hepatitis B virus immunopathology. Springer Semin Immunopathol. 1995;17(2-3):261-81. Review.	
	8	Citarella F, Misiti S, Felici A, Aiuti A, La Porta C, Fantoni A. The 5' sequence of human factor XII gene contains transcription regulatory elements typical of liver specific, estrogen-modulated genes. Biochim Biophys Acta. 1993 Feb 20;1172(1-2):197-9.	
	9	Crossley M, Ludwig M, Stowell KM, De Vos P, Olek K, Brownlee GG. Recovery from hemophilia B Leyden: an androgen-responsive element in the factor IX promoter. Science. 1992 Jul 17;257(5068):377-9.	
	10	Davies SE, Portmann BC, O'Grady JG, Aldis PM, Chaggar K, Alexander GJ, Williams R. Hepatic histological findings after transplantation for chronic hepatitis B virus infection, including a unique pattern of fibrosing cholestatic hepatitis. Hepatology. 1991 Jan;13(1):150-7.	
	11	Ding JW, Ning Q, Liu MF, Lai A, Leibowitz J, Peltekian KM, Cole EH, Fung LS, Holloway C, Marsden PA, Yeager H, Phillips MJ, Levy GA. Fulminant hepatic failure in murine hepatitis virus strain 3 infection: tissue-specific expression of a novel fgl2 prothrombinase. J Virol. 1997 Dec;71(12):9223-30.	
	12	Fischer et al., Journal of Virology, Feb, 1997, vol 71, No. 2, p. 996-1003.	
	13	Evans R, Kamdar SJ. Stability of RNA isolated from macrophages depends on the removal of an RNA-degrading activity early in the extraction procedure. Biotechniques. 1990 Apr;8(4):357-60.	
	14	Fickenscher H, Stamminger T, Ruger R, Fleckenstein B. The role of a repetitive palindromic sequence element in the human cytomegalovirus major immediate early enhancer. J Gen Virol. 1989 Jan;70 ( Pt 1):107-23.	
	15	Gasson JC. Molecular physiology of granulocyte-macrophage colony-stimulating factor. Blood. 1991 Mar 15;77(6):1131-45. Review. No abstract available.	
	16	Hardon, EM, Frain, M, Paonessa, G and Cortese, R. Two distinct factors interact with the promoter regions of several liver-specific genes. The Embo Journal 1998 vol. 7, No. 6, p.1711-1719	
	17	Keck JG, Stohlman SA, Soe LH, Makino S, Lai MM. Multiple recombination sites at the 5'-end of murine coronavirus RNA. Virology. 1987 Feb;156(2):331-41.	
	18	Keck JG, Soe LH, Makino S, Stohlman SA, Lai MM. RNA recombination of murine coronaviruses: recombination between fusion-positive mouse hepatitis virus A59 and fusion-negative mouse hepatitis virus 2. J Virol. 1988 Jun;62(6):1989-98.	
	19	Koyama T, Hall LR, Haser WG, Tonegawa S, Saito H. Structure of a cytotoxic T-lymphocyte-specific gene shows a strong homology to fibrinogen beta and gamma chains. Proc Natl Acad Sci U S A. 1987 Mar;84(6):1609-13	

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)			<b>Complete if Known</b>	
	Application Number	10/688,962		
	Filing Date	October 21, 2003		
	First Named Inventor	Gary Levy		
	Art Unit	1648		
	Examiner Name	Shanon A. Foley		
	Attorney Docket Number	9579-80		
Sheet	3	of	4	

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	20	Lai MM, Stohlman SA. RNA of mouse hepatitis virus. J Virol. 1978 May;26(2):236-42.	
	21	Lai MM, Cavanagh D. The molecular biology of coronaviruses. Adv Virus Res. 1997;48:1-100. Review. No abstract available.	
	22	Lai MM. RNA recombination in animal and plant viruses. Microbiol Rev. 1992 Mar;56(1):61-79. Review.	
	23	Lavi E, Murray EM, Makino S, Stohlman SA, Lai MM, Weiss SR. Determinants of coronavirus MHV pathogenesis are localized to 3' portions of the genome as determined by ribonucleic acid-ribonucleic acid recombination. Lab Invest. 1990 May;62(5):570-8.	
	24	Levy GA, Leibowitz JL, Edgington TS. Induction of monocyte procoagulant activity by murine hepatitis virus type 3 parallels disease susceptibility in mice. J Exp Med. 1981 Oct 1;154(4):1150-63.	
	25	Levy GA, MacPhee PJ, Fung LS, Fisher MM, Rappaport AM. The effect of mouse hepatitis virus infection on the microcirculation of the liver. Hepatology. 1983 Nov-Dec;3(6):964-73	
	26	Li C, Fung LS, Chung S, Crow A, Myers-Mason N, Phillips MJ, Leibowitz JL, Cole E, Ottaway CA, Levy G. Monoclonal antiprothrombinase (3D4.3) prevents mortality from murine hepatitis virus (MHV-3) infection. J Exp Med. 1992 Sep 1;176(3):689-97.	
	27	Mackman N, Fowler BJ, Edgington TS, Morrissey JH. Functional analysis of the human tissue factor promoter and induction by serum. Proc Natl Acad Sci USA. 1990 Mar;87(6):2254-8.	
	28	MacPhee PJ, Dindzans VJ, Fung LS, Levy GA. Acute and chronic changes in the microcirculation of the liver in inbred strains of mice following infection with mouse hepatitis virus type 3. Hepatology. 1985 Jul-Aug;5(4):649-60.	
	29	Makino S, Fleming JO, Keck JG, Stohlman SA, Lai MM. RNA recombination of coronaviruses: localization of neutralizing epitopes and neuropathogenic determinants on the carboxyl terminus of peplomers. Proc Natl Acad Sci USA. 1987 Sep;84(18):6567-71.	
	30	Makino S, Keck JG, Stohlman SA, Lai MM. High-frequency RNA recombination of murine coronaviruses. J Virol. 1986 Mar;57(3):729-37.	
	31	Masters PS, Sturman LS. Background paper. Functions of the coronavirus nucleocapsid protein. Adv Exp Med Biol. 1990;276:235-8. Review. No abstract available.	
	32	Miao CH, Leytus SP, Chung DW, Davie EW. Liver-specific expression of the gene coding for human factor X, a blood coagulation factor. J Biol Chem. 1992 Apr 15;267(11):7395-401.	
	33	Mizutani T, Maeda A, Hayashi M, Isogai H, Namioka S. Both antisense and sense RNAs against the nucleocapsid protein gene inhibit the multiplication of mouse hepatitis virus. J Vet Med Sci. 1994 Apr;56(2):211-5.	
	34	Ning Q, Brown D, Parodo J, Catral M, Gorczynski R, Cole E, Fung L, Ding JW, Liu MF, Rotstein O, Phillips MJ, Levy G. Ribavirin inhibits viral-induced macrophage production of TNF, IL-1, the procoagulant fgl2 prothrombinase and preserves Th1 cytokine production but inhibits Th2 cytokine response. J Immunol. 1998 Apr 1;160(7):3487-93.	
	35	Pachuk CJ, Bredenbeek PJ, Zoltick PW, Spaan WJ, Weiss SR. Molecular cloning of the gene encoding the putative polymerase of mouse hepatitis coronavirus, strain A59. Virology. 1989 Jul;171(1):141-8.	
	36	Parker MM, Masters PS. Sequence comparison of the N genes of five strains of the coronavirus mouse hepatitis virus suggests a three domain structure for the nucleocapsid protein. Virology. 1990 Nov;179(1):p. 463-8.	
	37	Sidwell, R.W., Huffman, J.H., Campbell, N. and Allen, L.B., Effect of ribavirin on viral hepatitis in laboratory animals. Ann.N.Y. Acad. Sci.284, 1977, p. 239-246	
	38	Parr RL, Fung L, Reneker J, Myers-Mason N, Leibowitz JL, Levy G. Association of mouse fibrinogen-like protein with murine hepatitis virus-induced prothrombinase activity. Journal of Virology. 1995 Aug;69(8):5033-8.	

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number

Substitute for form 1449A/PTO				<b>Complete if Known</b>	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (Use as many sheets as necessary)				Application Number	10/688,962
				Filing Date	October 21, 2003
				First Named Inventor	Gary Levy
				Art Unit	1648
				Examiner Name	Shanon A. Foley
Sheet	4	of	4	Attorney Docket Number	9579-80

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	39	Russell NH. Autocrine growth factors and leukaemic haemopoiesis. Blood Rev. 1992 Sep;6(3):149-56. Review.	
	40	Allen LB, Wolf SM, Hintz CJ, Huffman JH, Sidwell RW Effect of ribavirin on Type 2 Herpesvirus hominis (HVH/2) in vitro and in vivo. Ann N Y Acad Sci. 1977 Mar 4;284:247-53.	
	41	GenBank Accession No. M15761, Taxonomy Mouse fibrinogen-like protein gene, exon 1 gi 193303 gb M15761.1 MUSFIBLP1[193303]	
	42	GenBank Accession No. M35156, M.musculus Ig germline kappa-chain (Vk34C) gene V-region, exons 1 and 2 gi 197564 gb M35156.1 MUSIGKWW[197564]	

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<sup>1</sup> Applicant's unique citation designation number (optional). <sup>2</sup> Applicant is to place a check mark here if English language Translation is attached.

This collection of information is required by 37 CFR 1.98. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 120 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, VA 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

If you need assistance in completing the form, call 1-800-PTO-9199 and select option 2.